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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 22

Application Number: 09/714,883
Filing Date: November 16, 2000
Appellant(s): TURNER ET AL.

David W. Hibler
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 22 January 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein as sharing "structural similarity with animal ceruloplasmins" (page 2, lines 1-2) is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are

"useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to a DNA encoding a protein of as yet undetermined function or biological significance. It is clear from the instant application that the NHP (novel human protein) encoded by the claimed isolated nucleic acid molecule shares "sequence similarity with mammalian ceruloplasmins" (page 1, lines 11-12), which belong to a family of metal chelating proteins. It is known from the literature that "[c]erulloplasmins have been associated with development, ferroxidase activity, amine oxidase activity, copper transport, homeostasis, and superoxide dismutase activity" (page 1, lines 24-26). Based on the fact that NHPs of the instant application "share structural similarity with animal ceruloplasmins" (page 2, lines 1-2), it is suggested that the novel human proteins will play the same role as other mammalian ceruloplasmins. Thus, based on the structural similarities to a different protein, which belongs to a family of proteins with diverse and broad range of functions, it has been asserted that the NHP of the instant invention would also possess similar biological activities. Numerous publications exist on a topic that functional characteristics of a protein cannot be unequivocally extrapolated solely from its structural characteristics. According to fundamental principles of modern biology, the changing of one amino acid in a sequence gives, by definition, a new protein. One skilled in the art readily recognizes that in the absence of knowledge of a

biological significance of these particular NHPs encoded by the instant isolated nucleic acids the mere presence of "structural similarity with animal ceruloplasmins" would not be expected to be predictive of a specific and credible physiological function for the protein encoded by the claimed nucleic acids. The instant specification, as filed, fails to provide any information regarding a specific physiological function of the proteins encoded by the claimed isolated nucleic acids. A skilled artisan would not reasonably believe that a protein, which is described as having undisclosed structural similarity to animal ceruloplasmins, can be defined as an animal ceruloplasmin.

It is further asserted in the instant specification that agonists and antagonists of NHP expression "can be used as therapeutic agents for the treatment of any of a wide variety of symptoms associated with biological disorders or imbalances" (page 2, lines 21-23, emphasis added by the Examiner). It is also proposed to use "The NHPs or NHP peptides, NHP fusion proteins, NHP nucleotide sequences, antibodies, antagonists and agonists [...] for the detection of mutant NHPs or inappropriately expressed NHPs for the diagnosis of disease" (page 11, lines 19-22, emphasis added by the Examiner). Thus, based on the information provided in the instant specification, one skilled in the art would conclude that NHPs are asserted to be associated with practically any known disease or pathological condition. Such assertion would not be considered as specific or credible because it is not based upon evidence of record or sound scientific reasoning. Further, on page 12, lines 1-2, it is suggested to use the NHP products "as therapeutics (*i.e.*, for the treatment of Wilson's Disease, etc.)". The similarity of the disclosed NHPs encoded by the claimed nucleic acids to a family of proteins potentially associated with "disease" or Wilson's disease in particular does not make the instant DNA or encoded protein diagnostic of a

disease or useful in treatment of a disease. There is no evidence of record presented in the instant specification, which supports a conclusion that the instant nucleic acid or encoded protein is associated with any particular disease or disorder. To employ the claimed nucleic acids and NHPs encoded thereby in a method for identifying agonists and antagonist compounds that modulate the NHP expression or activity is not a substantial practical utility because it would relate to a protein for which no specific biological function is currently known. The instant application also fails to demonstrate use of the protein as a marker for any disease or condition, including Wilson's disease, which would be a real world use. Because the instant specification does not teach a biological activity of the protein, one cannot prevent or treat a pathological condition or a disease as implied by the specification.

Further, the instant specification fails to disclose a correlation between any specific disorder, including Wilson's disease, and an altered level or form of the claimed nucleic acids. Because the specification does not disclose whether the claimed polynucleotides would be overexpressed or underexpressed in a specific, diseased tissue as compared to a healthy tissue control one cannot employ the claimed nucleic acid in a diagnostic capacity in its currently available form. The specification contains assertions that the claimed polynucleotides can be used in "assessing gene expression patterns" (page 5, lines 5-6), which are used in the art for drug development and toxicology studies. However, without a disclosure of a particular disease or disease state in which the claimed polynucleotides are expressed at an altered level or form, one would be incapable of determining what the results of a particular gene expression patterns mean.

Thus, in the absence of knowledge of the specific biological significance of this particular nucleic acid and encoded protein, there is no immediately obvious patentable use for the claimed nucleic acid or the encoded protein. To employ a nucleic acid of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the encoded protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

Claims 1-3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

Appellant traverses the rejection of claims 1 to 3 for lack of utility on the premise that the rejection is in conflict with the decision in *In re Gay* stating that "there is no statutory requirement for the disclosure of a specific example". However, Appellant is mischaracterizing basis of the instant rejection. A specification can meet the legal requirements of utility and enablement for a new polynucleotide as long as the specification discloses at least one credible, specific and substantial asserted utility for the new polynucleotide, or a well-established utility

for the claimed polynucleotide would be *prima facie* obvious to the skilled artisan. A hypothetical example may serve to clarify. For example, a hypothetical specification discloses that a claimed polynucleotide is expressed in colon cancer and not expressed in healthy colon tissue. The hypothetical specification does not disclose the biological activity of the polypeptide encoded by the polynucleotide. The claimed polynucleotide in the hypothetical example would not be rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as it has utility and is enabled as a colon cancer marker. However, such is not the fact pattern here. The instant specification discloses that the claimed nucleic acids encode proteins that are in general structurally related to animal ceruloplasmins and hypothesizes that the detection of claimed polynucleotides can be used for the diagnosis of a disease, or, for example, Wilson's disease. However, there is no disclosure that the claimed polynucleotides are expressed at altered levels or forms in any specific, diseased tissue or otherwise associated with any particular disease including Wilson's disease, as implied by the instant specification. It is noted that no evidence has been brought forth during the prosecution history regarding the expression levels of NHPs encoded by the claimed nucleic acids in diseased or healthy tissue. Also, no evidence has been brought forth that the claimed polynucleotides encode polypeptides have a specific activity associated with any disease. Thus, the examiner has concluded that the assertion of the utility of the claimed nucleic acids as being associated in general with biological disorders is not specific and, further, that the assertion of the association with Wilson's disease is not credible.

Beginning at p. 4, second paragraph, of the Brief, Appellant argues that the utility of the claimed polynucleotide can be imputed based on the fact that the amino acid sequences encoded by the claimed nucleic acids share 57% sequence identity with human ceruloplasmin and submits

a statement that based on this structural similarity one of ordinary skill in the art would clearly conclude that Appellant's sequence is a ceruloplasmin. This argument has been fully considered but not found to be persuasive because a skilled artisan, upon consideration the limited degree of sequence similarity between a protein of the instant invention and human ceruloplasmin, would only conclude that a protein that has almost as many structural differences as similarities with that human ceruloplasmin, would be expected to, at most, belong to the same family of the metal chelating proteins as ceruloplasmins or be of the same evolutionary origin as human ceruloplasmin. One skilled in the art would not conclude that the protein of the instant invention is ceruloplasmin. To clarify, the examiner never asserted that NHPs encoded by the claimed nucleic acids and ceruloplasmins are unrelated. They are clearly structurally related. However, the rejection sets forth that, *among related polypeptides* in protein families, limited structural similarity alone is not predictive of functional similarity. There are no known teachings in the modern art that would allow one to make a definitive prediction of a specific function for a protein solely based on a limited molecular similarity or homology to another protein with known function. Moreover, one skilled in art readily recognizes the existence of numerous proteins that share some similarity to human ceruloplasmins at the level of 50%; however, most of these proteins are clearly not human ceruloplasmins.

Furthermore, as Appellant returns to the discussion of the association of the claimed nucleic acids with Wilson's disease, at page 4, last paragraph, it is clear from the prior art that the specific function of ceruloplasmins in etiology or progression of Wilson's disease has also not been established at the moment. Appellant argues that the relationship between ceruloplasmins and Wilson's disease is well established in the art and refers to the article of

Chowrimootoo et al. (Exhibit D of the Brief), which allegedly establishes that different ceruloplasmin isoforms serve as an accurate marker for Wilson's disease. However, the publication of Chowrimootoo et al. clearly indicates that only some of the ceruloplasmin isoforms may be associated with Wilson's disease (see abstract and also column 2 on page F198), and no other art was found to support Appellant's assertion regarding a clear nexus between ceruloplasmins and Wilson's disease. Furthermore, once again, any argument regarding association of ceruloplasmins and Wilson's disease is not applicable in the instant case due to the fact that the claimed nucleic acids do not encode human ceruloplasmins. There is no evidence of record to support the conclusion that the instant NHPs encoded by the claimed nucleic acid is a human ceruloplasmin associated with Wilson's disease.

Beginning at the second paragraph of p. 5 of the Brief, Appellant summarizes case law on the utility requirement. The essential disagreement appears to be the interpretation of *In re Brana*, 51 F.3d 1560,1566, 34 USPQ2d 1436 ,1441 (Fed. Cir. 1995). That court decision determined that a compound which belonged to a family of compounds known to have anti-tumor activity, which is a common and well established specific and substantial utility for that family of compounds, would be reasonably expected to have anti-tumor activity in light of positive *in vitro* data with respect to that particular compound since that data has proven to be an indicator of anti-cancer activity by other members of that family. The protein of the instant invention clearly does not belong to a family of compounds with a common well-established specific and substantial utility. The utility of those members of the ceruloplasmin family of metal chelating proteins, to which the protein encoded by the claimed nucleic acid appears to belong, lies in the knowledge that they each "have been associated with development,

ferroxidase activity, amine oxidase activity, copper transport, homeostasis, and superoxide dismutase activity" (page 1, lines 24-26). Moreover, again, there is no evidence of record or sound scientific reasoning presented that would provide support for the conclusion that the instant NHPs possess any of the known biological activities of specific ceruloplasmins. There is no *in vitro* data provided in the instant specification that would be accepted as predictive of *in vivo* results, and there is no description of the clinical administration of NHPs of the instant invention. Therefore, the examiner maintains the position that Appellant's reliance on *In re Brana* is misplaced.

Appellant's reliance on case law pertinent to 35 USC § 112, first paragraph, is also misplaced because the instant rejection is a utility and not an enablement rejection. 35 USC § 101 clearly states that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. The fact that Appellant submits that some experimentation may be required to practice the claimed invention simply confirms that the instant invention was not completed as filed, and, therefore, clearly lacks utility in currently available form.

Appellant further argues at page 7 of the Brief that "the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips". The employment of the nucleic acids of the instant invention in a DNA chip is not a substantial or specific utility. Regarding the merit of the argument, any naturally occuring polynucleotide can be used in a DNA chip, and thus this asserted utility is not specific. The instant specification does not substantiate a link between the claimed polynucleotides and any specific disorder. The specification merely discloses that the claimed polynucleotide encodes a

protein that is structurally related to animal ceruloplasmins, and that it is expected to be involved in a disease, for example, Wilson's disease. The specification does not provide any evidence that the claimed polynucleotide is expressed at an altered level or form in any diseased *versus* healthy tissue. In the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the polynucleotide itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

Appellant argues that specific utility of the claimed nucleic acids when used in a DNA chip is justified because of their "well-established medical relevance" (page 7, middle of the page). This has not been found to be persuasive for the reasons fully explained earlier. Briefly, the disclosure that the instant NHPs are structurally related to ceruloplasmins does render the asserted utility specific, since the specification does not establish that NHPs are expressed in any diseased tissues in any way that is different from the way they are expressed in healthy forms of the same tissues. In other words, the specification does not disclose that the NHPs themselves are expressed in tissues associated with any disease, including Wilson's disease, at altered levels or forms. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify diseases or disease states which correlate with altered levels or forms of the claimed polynucleotides. Therefore, this asserted utility is not applicable to the claimed invention in its currently available form.

Furthermore, to accept Applicant's arguments that "the present nucleotide sequence has a specific utility in determining the genomic structure of the corresponding human chromosome"

(page 8, second paragraph of the Brief) and are therefore useful would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object. It was just such applications that the court appeared to be referring to when it expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)). Because the steroid compound, which was the subject of that decision had a known structure and molecular weight it could have readily been employed as a molecular standard at that time. Further, because that compound was a hydrocarbon it certainly could have been employed in the well-known process of combustion for purposes of lighting and/ or the generation of heat. The generation of heat by combustion of hydrocarbons certainly was and remains an important process. Irrespective of such obvious utilities, the court still held that the compound produced by the process at issue in *Brenner v. Manson* did not have a specific and substantial utility (emphasis added).

To grant Applicant a patent encompassing an isolated polynucleotide encoding a naturally occurring human protein of as yet undetermined biological significance would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" *Brenner v. Manson, Ibid*). To grant Applicant a patent on the claimed polynucleotide based solely upon an assertion that it can be employed in a DNA chip is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted and would be no different than granting a patent on the process

disputed in *Brenner v. Manson* on the premise that the steroid produced thereby was useful as an analytical standard or as a fuel source.

Finally, in response to Appellant's arguments that patents have been issued to similar subject matter (last paragraph at page 9 of the Brief), it is well settled that the prosecution of one patent application does not affect the prosecution of an unrelated application. *In re Wertheim*, 541 F.2d 257, 264, 191 USPQ 90, 97 (CCPA 1976) (holding that "[I]t is immaterial in *ex parte* prosecution whether the same or similar claims have been allowed to others"). Accordingly, Appellant's arguments with respect to the other patents issued by PTO are unavailing.

Therefore, for reasons set forth above, Appellants arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility and it is believed that the rejections should be sustained.

Respectfully submitted,

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March 27, 2003 OC

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